

Point/Counterpoint: Nerve Decompression in Diabetic Peripheral Neur

If we can surgically decompress patients with active entrapment,
we may be able to alleviate their pain.

BY A LEE DELLON, MD

As a young surgeon, I treated patients with carpal tunnel syndrome, and many of these patients had diabetes. They would ask, “Can you help my feet?” I confessed at the time that I did not know that much about feet.

How does what we see in the hand relate to what we see in the foot? People have numbness in their fingers and hands, which bothers them at night and they feel like their whole hands are numb. They get clumsy and they drop things. This numbness is very similar to what people with diabetic peripheral neuropathy (DPN) complain about in reference to their feet.

The randomized controlled trials that have been done and are ongoing have not given us a real solution for DPN. How can I help these people with painful symptoms?

IDENTIFICATION TOOLS NOT GOOD ENOUGH

We know that we must identify patients with DPN early using methods such as calibrated tuning forks and biothesiometers. These tests to evaluate the peripheral nervous system have been in practice for many years, however, they use estimates and algorithms. There are many criticisms of these classical tests. For example, as surgeons we want to distinguish the perineal nerves from the tibial nerve. You cannot do this with vibration detection threshold because it stimulates both nerves.

The two-point discrimination tells us about intervention density, and in 1985 we created a device to make it easier to test. Later, with an aerospace engineer to help evaluate the outcomes from our surgery, we developed a new device: the pressure-specified sensory device. In an early article, we showed that diabetics with ulcerations had poorer sensory results than diabetics without ulcerations.

When we look at the authorities on DPN, this sums it up and has for many years: We do not actually have anything that we can do for the patient. So, I applied the concept of decompressing multiple peripheral nerves in the extremity of a patient. Some patients can wake up in the recovery room and feel some sort of improvement. This helped us refine our hypothesis: Symptoms of DPN — in some patients — are due to compression of peripheral nerves. If this is true, the corollary will be that the symptoms of DPN in some patients are reversible by decompressing of those peripheral nerves.

INVESTIGATING THE HYPOTHESIS

In 1992 we published a study of 60 diabetic patients. The included cohort had to have a positive Tinel’s sign to signify the superimposed entrapments and no ulcer or amputation. In this group, 8% were said to be normal and 11% had localized entrapment, with the rest having diffuse peripheral neuropathy. Some patients were caught early enough that they were identified with the traditional testing of superimposed nerve compressions. We operated on these people, decompressing a total of 154 different nerves, and they were followed for an average of 30 months. In the total cohort, 88% were improved. In the group that had localized compression, 100% of them were healed completely. The group that had neuropathy with superimposed compressions had 80% improvement and in the group that had diffuse neuropathy, 50% were better. Criticisms? I evaluated my own patients, and I am clearly biased. Also, maybe there was a placebo effect.

In the laboratory, we looked at the basic science work. We studied the pathophysiology of nerve compression in rats and monkeys using a tube that was relatively long with respect of the diameter of the nerve. After 6 months of compression, we saw thinning of the myelin. By 1 year, we have

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the Management of neuropathy: Is There Evidence?

There is clearly a place for surgery in the treatment of common or “garden variety” diabetic neuropathy ... it is just that I have not been able to find it.

BY AARON I. VINIK, MD, PhD

The real issue with regard to nerve compression and the diabetic patient is should we be doing decompression surgery for diabetic peripheral neuropathy (DPN) as opposed to surgery for entrapment syndromes? While Dr. Dellon’s presentation may have been very eloquent, we have to ask whether the argument can be translated into care of the patient with diabetes.

The clinical presentation of DPN is that it involves small and large somatic and autonomic nerve fibers with an increased incidence (30%) of entrapment. According to the recent position statement of the American Diabetes Association, to make the diagnosis of DPN there must be more than two abnormalities, such as on neurological examination, nerve conduction study, quantitative autonomic function, quantitative sensory or quantitative motor function. The diagnosis of entrapment requires electrophysiologic evidence of a conduction block at the site.

Many people believe diagnosis is a relatively simple task and that we can all do this. But, let us look at the mistakes we have all made with this diagnosis. With mild neuropathy, in which there is a potential for reversal of the situation, the diagnosis is missed 65% to 70% of the time. We still need to improve our ability to recognize the symptoms. We mistake osteoarthritis, Charcot neuroarthropathy, diabetic neuropathy, plantar fasciitis, tarsal tunnel syndrome and fibromyalgia as DPN. Failed clinical trials for DPN can be ascribed to this negligence to define the cause of the pain.

MEASURING OUTCOMES

How do we measure outcomes? The symptoms must improve to a significant degree, and it must not be due to worsening of neuropathy. We need to be sure we are not creating a deterioration of nerve function. The change, if possible, should correlate with evidence of improved nerve func-

tion such as nerve conduction, intraepidermal nerve fiber, quantitative sensory and quantitative autonomic function tests. The change should be biologically relevant, based upon the view that this is what patients interpret as clinically meaningful. The treatment being evaluated should have a low number needed to treat, but more importantly a high number needed to harm (*primum non nocere*)!

Objective measures of responsiveness. There are different scoring systems for evaluating neuropathy, eg Dyck’s Neuropathy Symptom Score (NSS), Neuropathy Disability Score (NIS) and the Neuropathy Impairment Score of the Lower Limbs (NISLL). You can also use a simpler neuropathy disability score such as Eva Feldman’s Michigan Neuropathy Scoring System. We should attempt to relate the clinical score to the nerve function. In addition, quantitative measures for threshold of vibration, thermal perception, heat pain, cold pain, touch pressure and nerve conduction can be obtained.

We developed receiver operating characteristics measuring the area under the curves for sensitivity and specificity of small and large fiber function tests. The vibration detection threshold gives about 90% sensitivity if the specificity is held at >90%. It is important to remember that different measures measure very different things, and that the test must be validated for sensitivity, specificity, reproducibility, accuracy and to be able to show a change with therapy. Two-point discrimination has not met these criteria.

ENTRAPMENT OR SOMETHING ELSE?

Can we tell the difference between entrapment versus DPN or entrapment superimposed on DPN? My colleagues and I have looked at the frequency of entrapment of the tibial nerve in 4,600 patients. If the latency of the perineal and the tibial nerves are equal, then the diagnosis is DPN. If

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continued thinning and dropout of large myelinated fibers. We can surgically decompress this nerve and regain fibers, although the myelin does not recover its previous thickness.

LINK BETWEEN DIABETES AND COMPRESSION

One important implication when it comes to evaluating our patients is that over time, their symptoms are going to change. Why would diabetes predispose the nerve to chronic compression? First, the nerve is swollen. The nerve swells in a tight anatomic area, and we can postulate decreased blood flow and chronic compression. There is decreased ectoplasmic flow, and this is a slow component that means that building blocks are delayed and the nerve has to repair itself distally. We applied our chronic decompression model and showed that a diabetic banded rat was more likely to have nerve compression and be worse than the nonbanded rat.

Our hypothesis is that the symptoms are related to nerve compression. Prospective studies from what you might term a loose meta-analysis of the 14 published studies, all with the same inclusion criteria, operative technique and outcome measures, have shown good results. We have a cohort of 833 patients with this degree of magnitude of improvement and no new ulcers or amputations.

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nance can improve detection thresholds for pressure and vibration⁸ or even tactile coactivation.⁹ If only symptoms are being reported, as has occurred in the 12 reported studies, this may be no better than magnet-field therapy,¹⁰ percutaneous electrical nerve stimulation¹¹ or infrared therapy.¹² all of which have been claimed to achieve improvement in symptoms at least on a short-term basis and are noninvasive. Additionally, the results of several large 6- to 12-month clinical trials of diabetic neuropathy have been besieged by the placebo effect (Vinik Medscape) in which there have been improvements not only in symptoms but in objective measures of neuropathy presumably related to better hygiene, cessation of smoking, the use of statins and ACE inhibitors among the possible variables that affect the symptom complex of neuropathy (Tessfaye ADA abstract). An extreme example of the placebo effect involved the Middlesex Hospital when 194 patients were placed on a waiting list for arthroscopy. Eighty seven (67 men) had waited >1 year with suspected meniscal tears, degenerative joint disease, ligamentous instability and sundry other complaints. At the end of a year 67% of patients who had not had surgery had recovered spontaneously!

In summary, tarsal tunnel release is being advocated as a procedure for common or garden DPN in the absence of entrapment even if there is no sign of recoverable nerve function!¹³ Unfortunately the studies reported have been of poor quality and design and it has not been possible to discern the differences in patients being treated who have only DPN from

NEW MULTICENTER TRIAL

We have trained 260 surgeons in 42 states in the United States, and 36 of these have begun entering patients into a prospective multicenter study available on the Internet at neuropathyregistry.com. So far, there are 549 patients and 40% have had their second side done. We have seen no new fractures in this group of patients.

How do we select the patient with superimposed compression? We use a positive Tinel's sign, as simple as that sign is. In this group of patients, remember before we had 69% improvement. Now, we have a positive Tinel's sign being a positive predictive value of 92%.

If we can decompress patients with active entrapment — and there are many patients with this condition — we may be able to improve their symptoms. ■

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those who have an entrapment who might indeed have benefited. The standard testing of the individuals has not been blinded and only within subjects studies are reported which are notoriously unreliable. Standard testing of distal sensory loss of small and large fiber function, eg VDT and thermal perception, strength, reflexes and nerve conduction using validated instruments would be helpful. There is a need to grade severity of entrapment, use measures of sensory tests that have been validated, the presence of a Tinel's sign, the presence of motor features and atrophy before considering surgery.¹⁴

We would recommend that before considering surgery the following caveats should be added:

- A conduction block must be present at the site proposed for decompression;
- There should not be such severe neuropathy as to preclude distinction from entrapment;
- Control sham operations should be compared with decompression for relief of symptoms if these are the only measure made; and

Objective standardized measures should be employed before and after the intervention to show bona fide improvement in nerve function.

As pointed out in a recent report from the American Academy of Neurology (*Neurology*. 2006;66:1805-1808) the utility of surgical decompression for symptomatic diabetic neuropathy would in their minds receive a Grade 1V rating, ie evidence from uncon-

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there is a discrepancy on either side, then there may be entrapment. We found that carpal tunnel syndrome was very common, and that evidence of entrapment of the tibial nerve superimposed on DPN was extremely rare.

In DPN, one sees edema of the canal with atrophy of the small muscles of the feet. What comes first? One of the major causes of DPN is microvascular insufficiency in which damage to the blood vessels by impaired function or occlusion decreases blood supply to both myelinated and unmyelinated nerve fibers. Can one recognize the patient with compression in the tunnel in the face of DPN? This may be extremely difficult.

Do we know its entrapment? Let's look at the clinical features of 1,528 hands with a neurological diagnosis of carpal tunnel syndrome; symptoms were not restricted to the hand in 31% of cases. Conclusions were wrong 40% of the time, pain was not as reliable as paraesthesiae and Tinel's sign was positive only 34% of the time. False positives in this group occurred in patients with fibromyalgia and tendonitis. In fibromyalgia there is a large proliferation of the small intraepidermal nerve fibers — the opposite of what occurs in DPN.

Is improvement due to the intervention? What about the placebo effect? Why do you see improvement in people when you operate on them, and they come out one day later and tell you everything is better? Are there ways to

cure people using nonsurgical methods such as stochastic resonance, magnetic therapy and infrared therapy? You can enhance sensation in the diabetic neuropathic foot with mechanical noise or vibration prior to testing. In these studies, however, there is no real measure of improvement, but simply a measure of changing the detection of a modality.

Dr. Dellon, however, found a 20% failure of the predictive value of a Tinel's sign. When I touch, vibrate or add pressure to one foot, the threshold in the other limb changes. So, now when I am trying to do this, if I stimulate the other limb, I will produce a reduction in the patient's ability to perceive. Now, if I stimulate the same limb, I will improve the patient's ability and if I stimulate the same limb further with noise plus measuring two-point discrimination, I will now give the patient a greatly enhanced two-point discrimination. So, this says to me, can I really trust this as a measure of what I am looking at, when I can do this with noise?

Could we possibly do damage with surgery? If you have good nerve function, you have pain. But, if you damage the system when you have pain and are through the pain threshold, pain can also disappear. We do not want to take people who have intraepidermal nerve fibers and no pain, from people who have a slight decrease and they have pain, to people who have a disappearance of pain because of complete clearance of the nerve fibers. Do not do things that potentially may hurt.

CONCLUSIONS

Decompression of multiple nerves in diabetes are being advocated by some surgeons for the treatment of common or *garden-variety* DPN. There is a need to grade the severity of entrapment, use measures of sensory tests that have been validated, the presence of a Tinel's sign, the presence of motor features and atrophy before considering surgery. A conduction block should be present, and there should not be severe neuropathy to preclude distinction from entrapment. Control and sham operations should be compared in order to determine outcomes from these procedures. Sham operations should be compared with unentrapment operations for symptoms if they are the only measure of the change, and objective standardized measures should be employed to show improvements in nerve function.

There may be a place for surgery in the treatment of common or garden-variety diabetic neuropathy. It is just that I have not been able to find it. ■

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trolled studies, case reports or expert opinion and assign the evidence a U grading which translates to unproven, the data being conflicting given the current knowledge and treatment not recommended at this point in time. Thus as I have previously concluded "there may be a place for surgical decompression of nerves in DPN but we have yet to find it." ■

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